REPLACEMENT SHEET

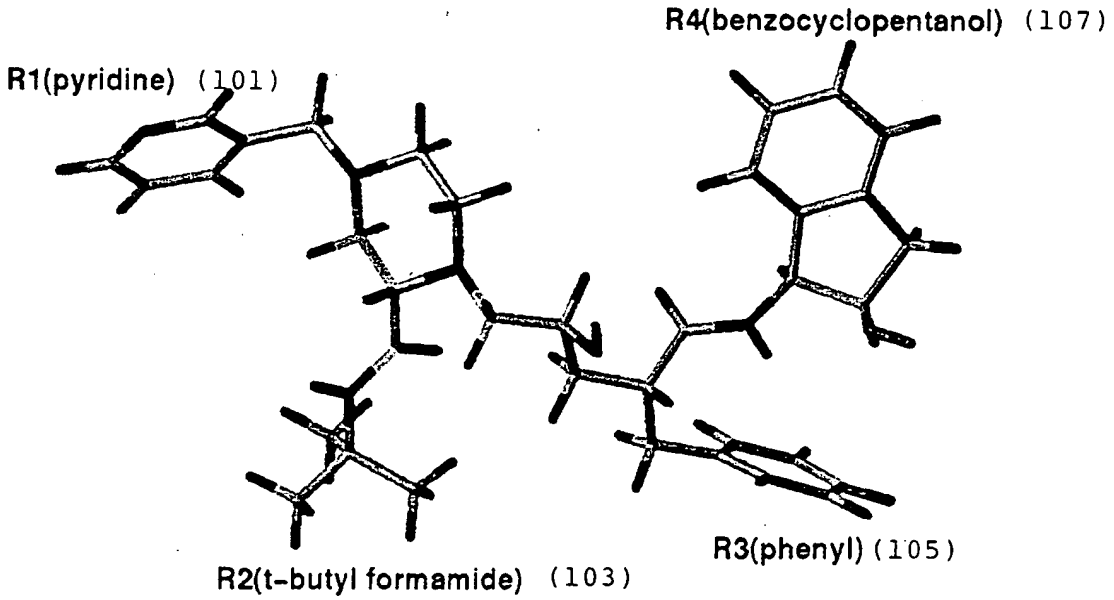


FIG. 1

REPLACEMENT SHEET

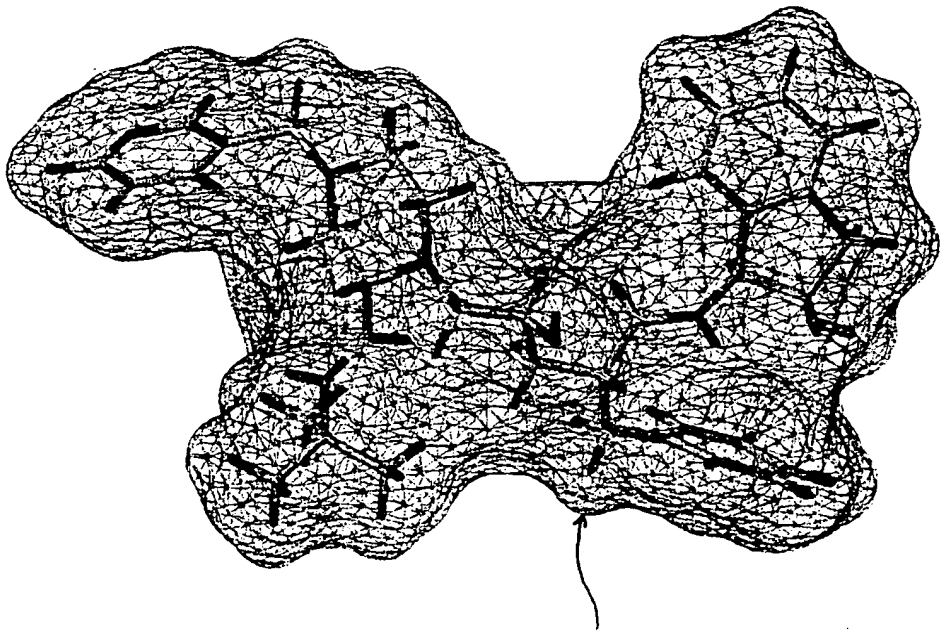


FIG. 2

REPLACEMENT SHEET

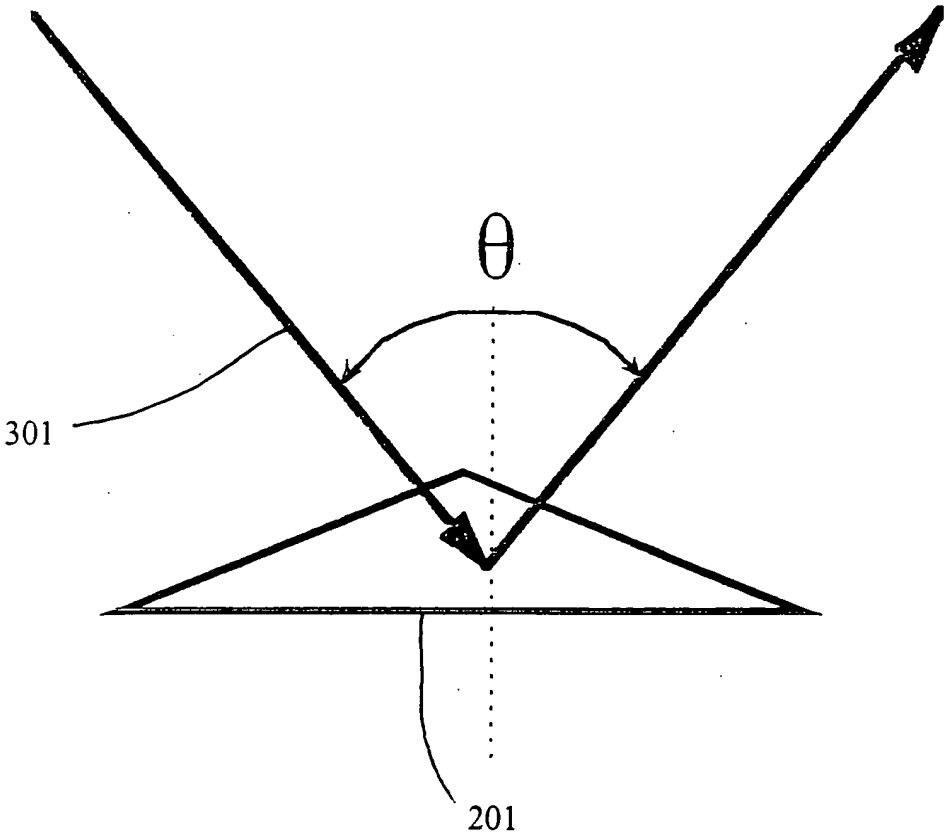


FIG. 3

REPLACEMENT SHEET

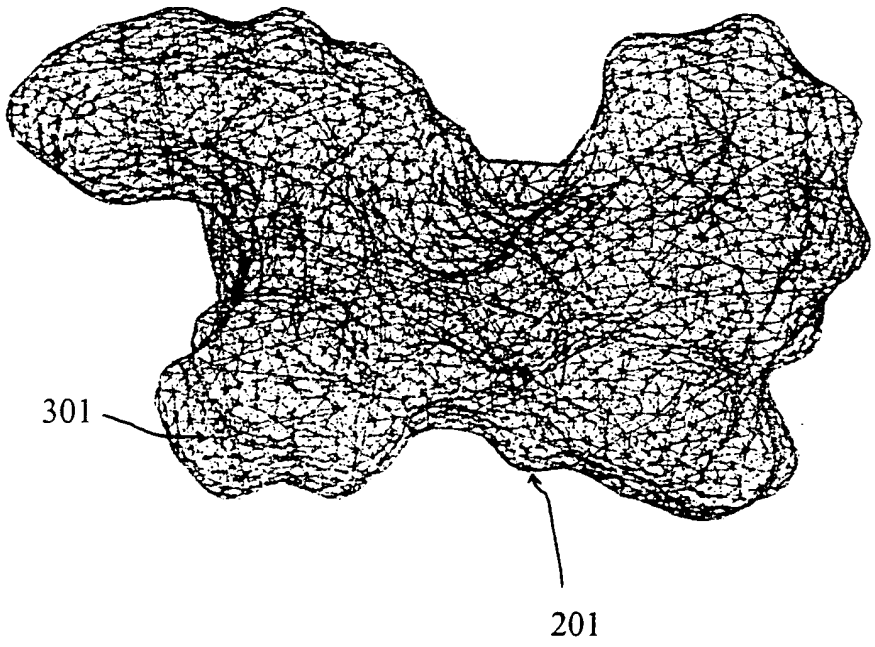


FIG. 4A

REPLACEMENT SHEET

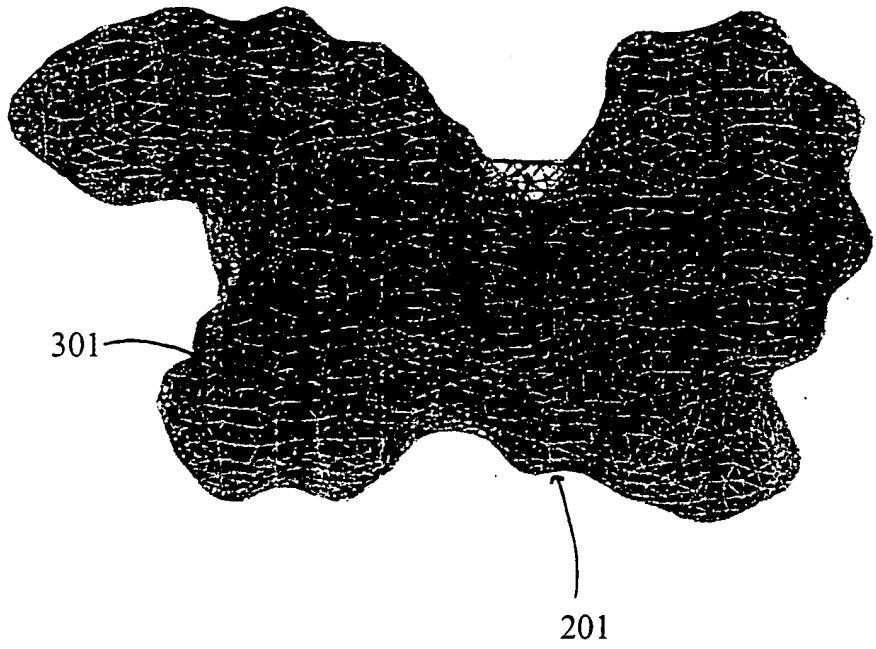


FIG. 4B

REPLACEMENT SHEET

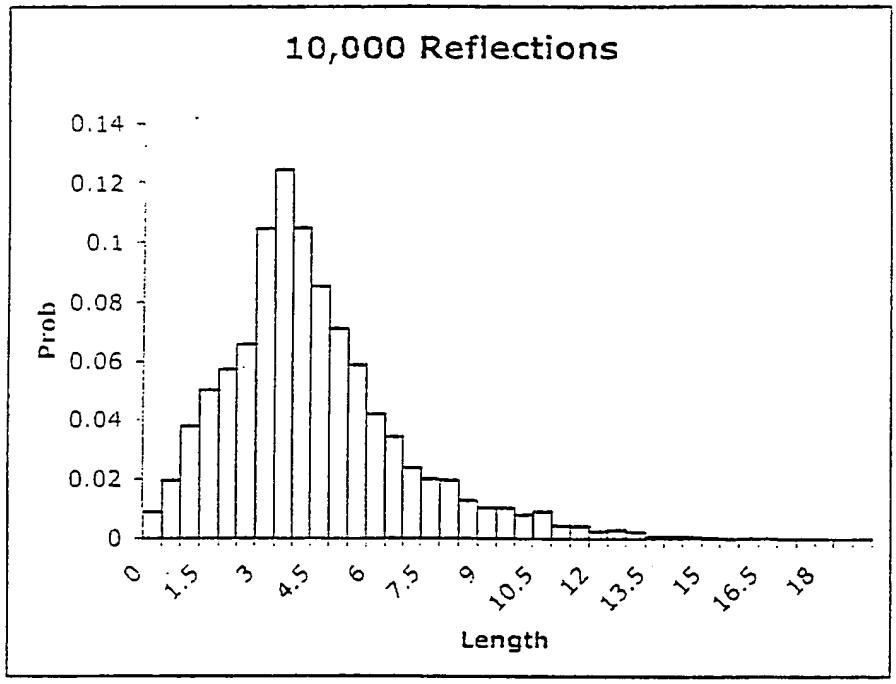


FIG. 5A

REPLACEMENT SHEET

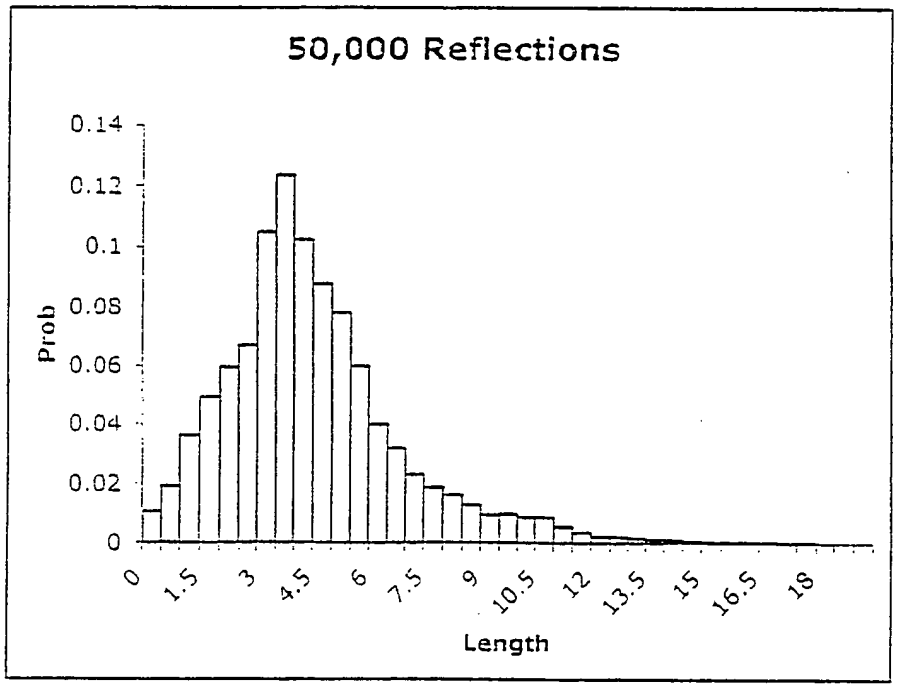


FIG. 5B

REPLACEMENT SHEET

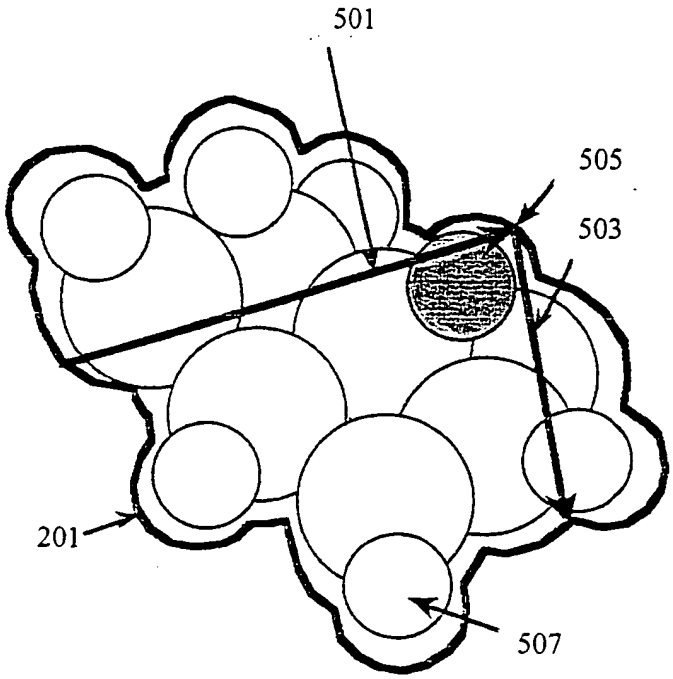


FIG. 6

REPLACEMENT SHEET

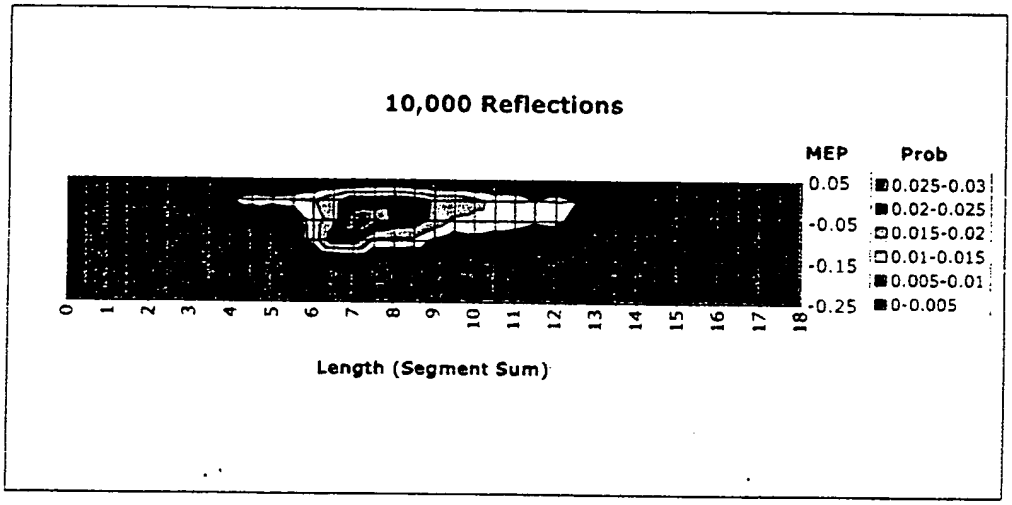


FIG. 7A

REPLACEMENT SHEET

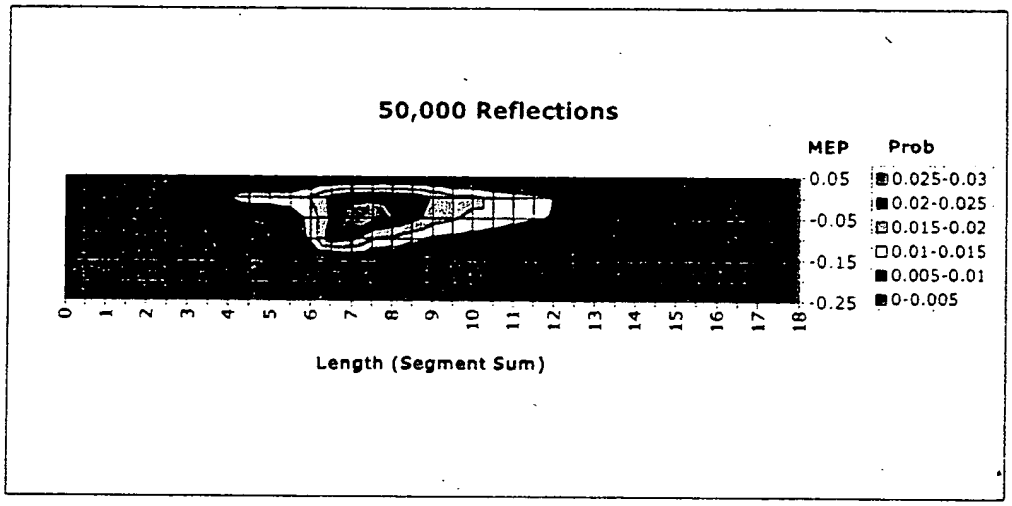


FIG. 7B

REPLACEMENT SHEET

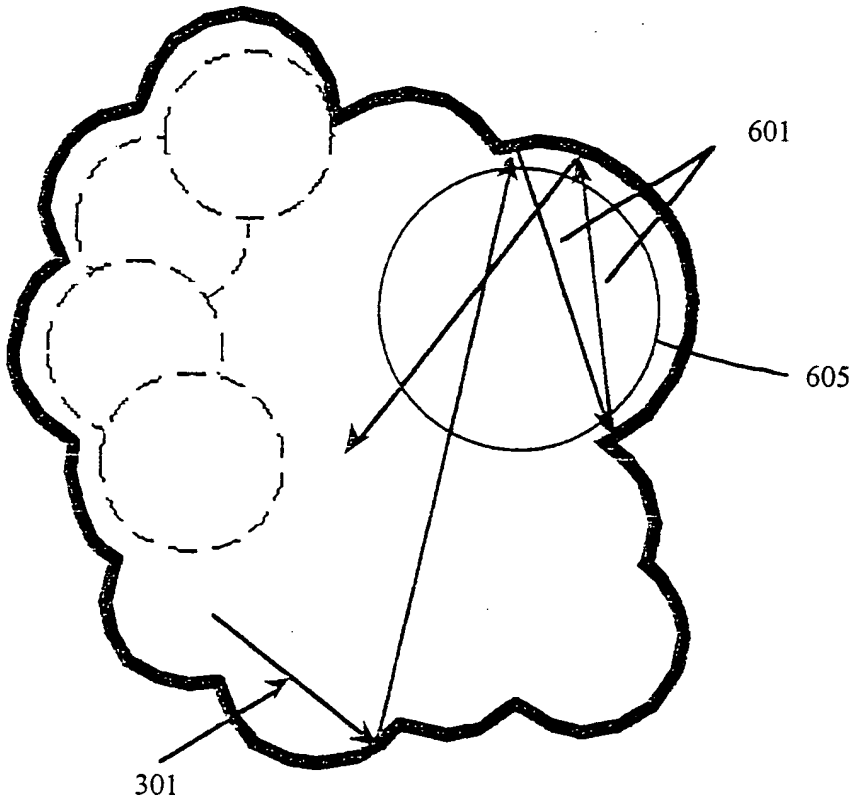


FIG. 8

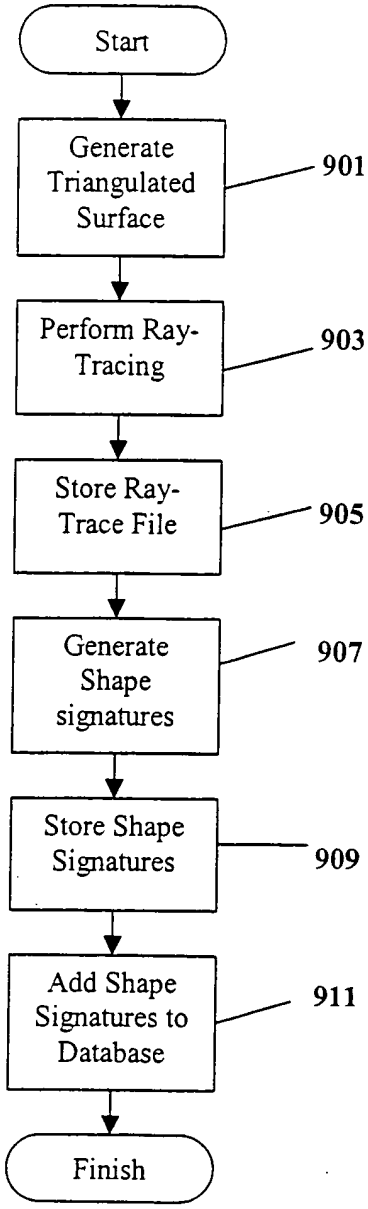

Start
Generate Triangulated Surface
901
Perform Ray-Tracing
903
Store Ray-Trace File
905
Generate Shape signatures
907
Store Shape Signatures
909
Add Shape Signatures to Database
911
Finish

FIG. 9

REPLACEMENT SHEET

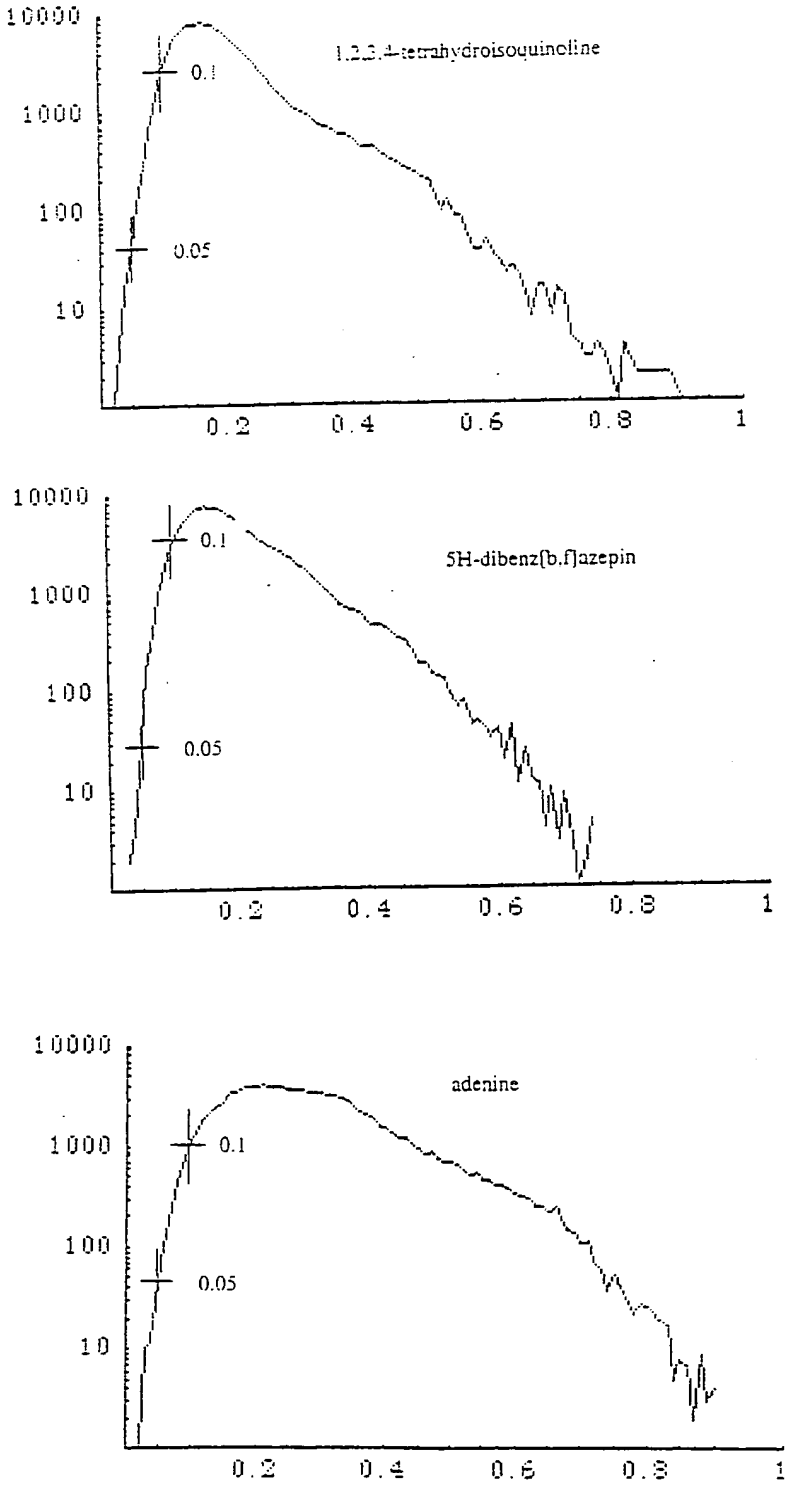


FIG. 10A

REPLACEMENT SHEET

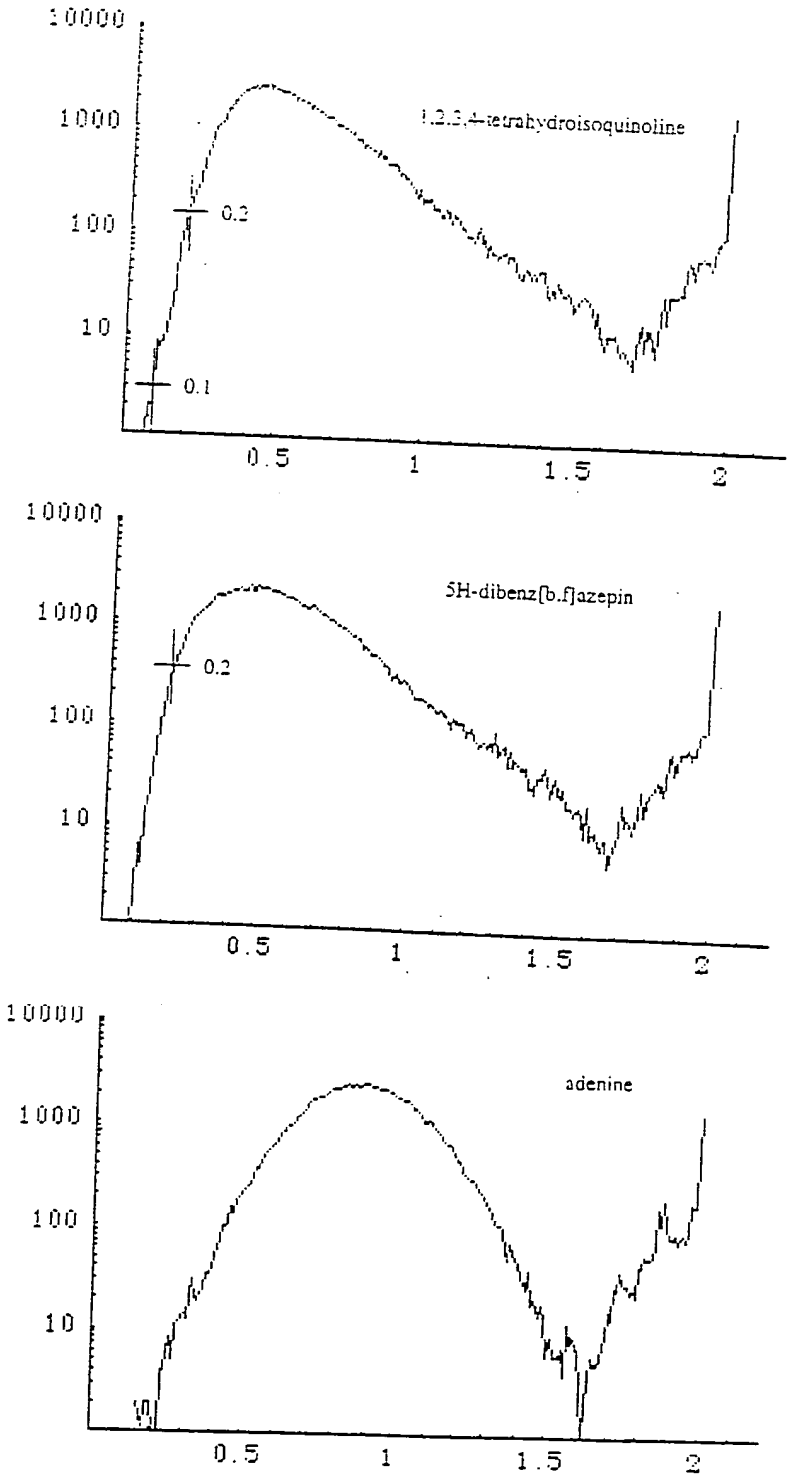


FIG. 10B

REPLACEMENT SHEET

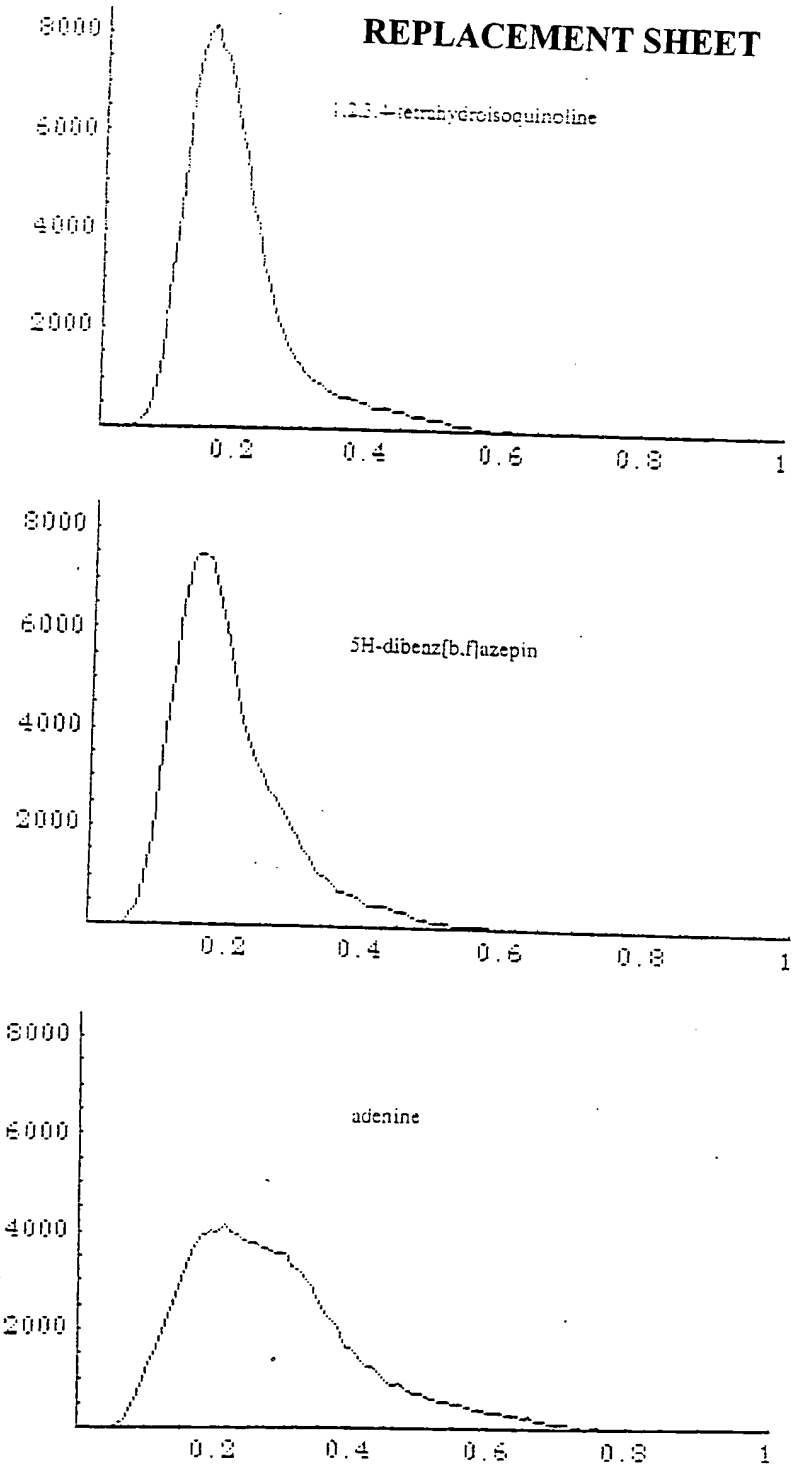


FIG. 11A

REPLACEMENT SHEET

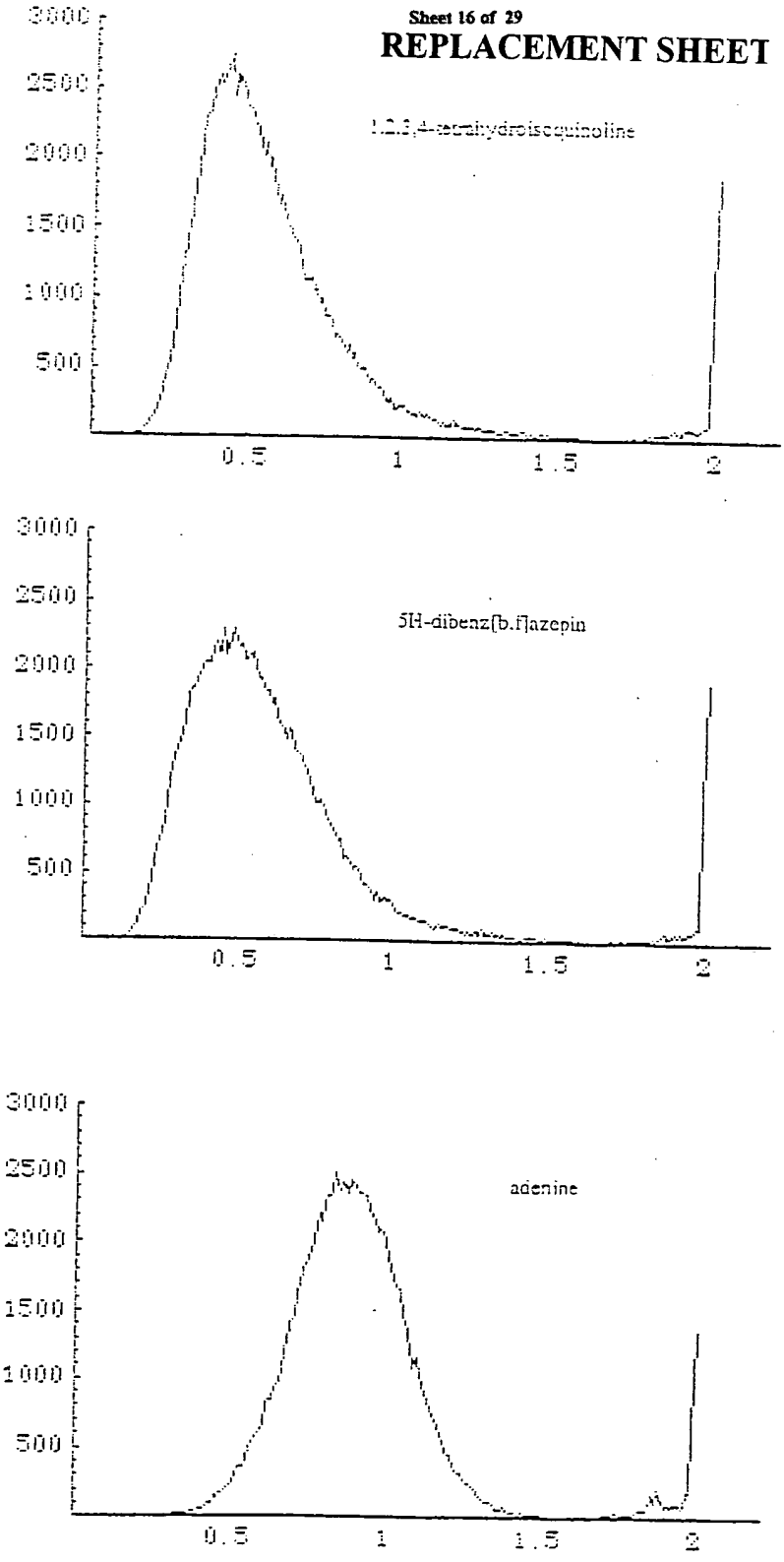


FIG. 11B

REPLACEMENT SHEET

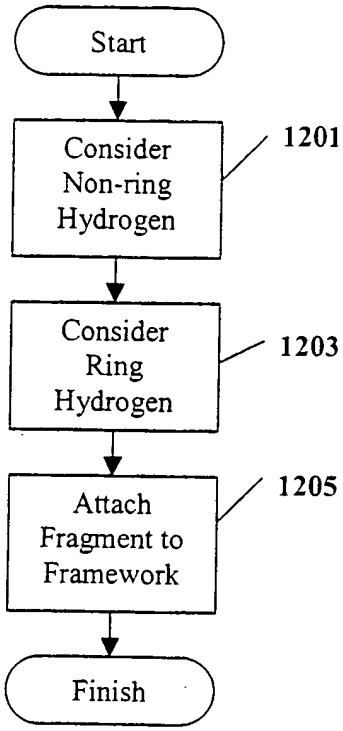


FIG. 12

REPLACEMENT SHEET

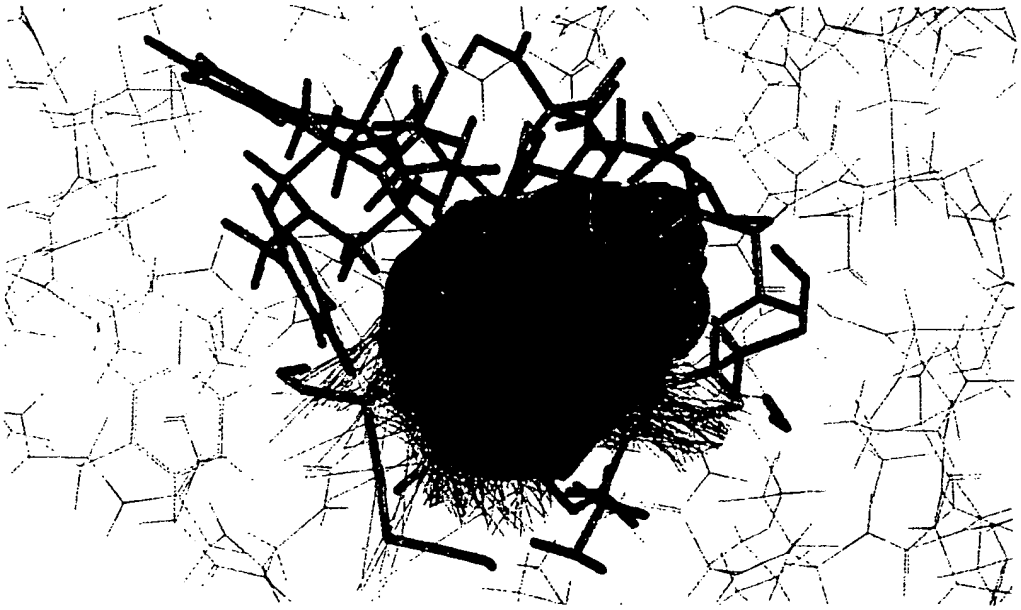


FIG. 13A

REPLACEMENT SHEET

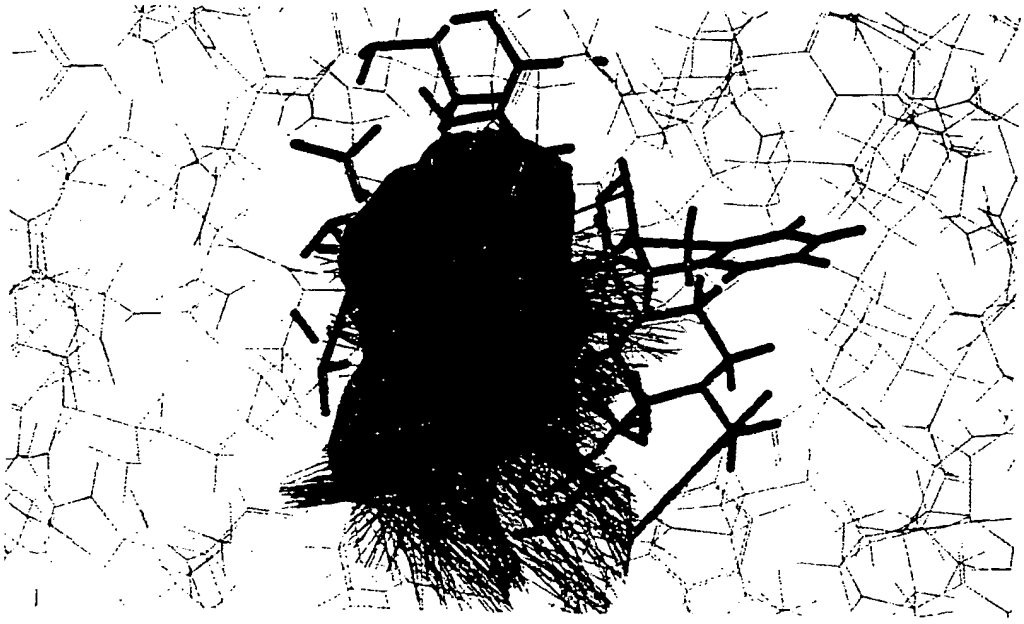


FIG. 13B

REPLACEMENT SHEET

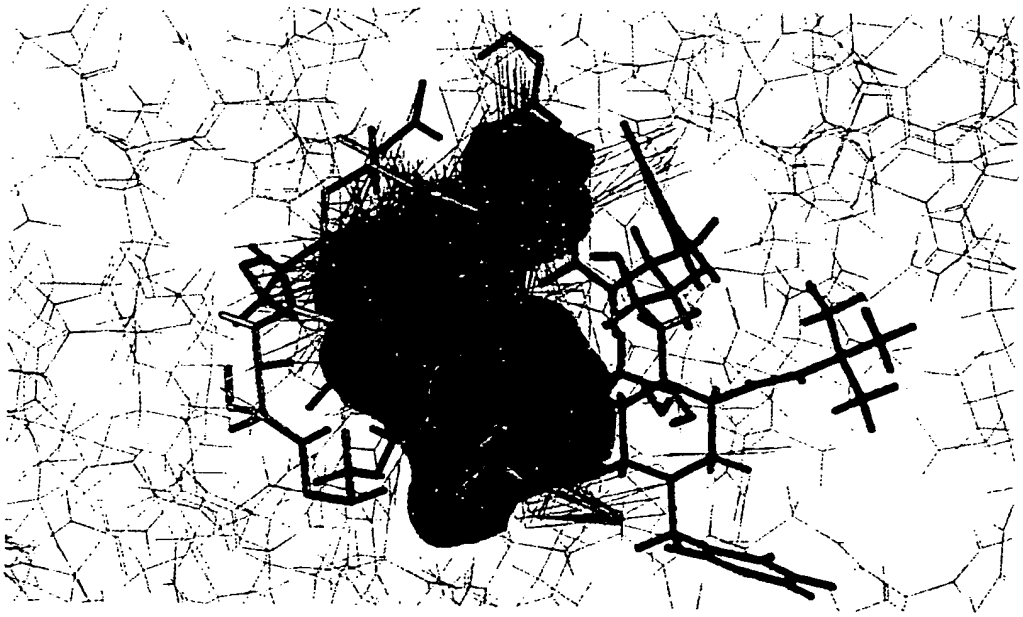


FIG. 13C

Results for Six Query Compounds, 1-D Shape Signature Self-Comparison of Tripos Fragment using L_1 Metric

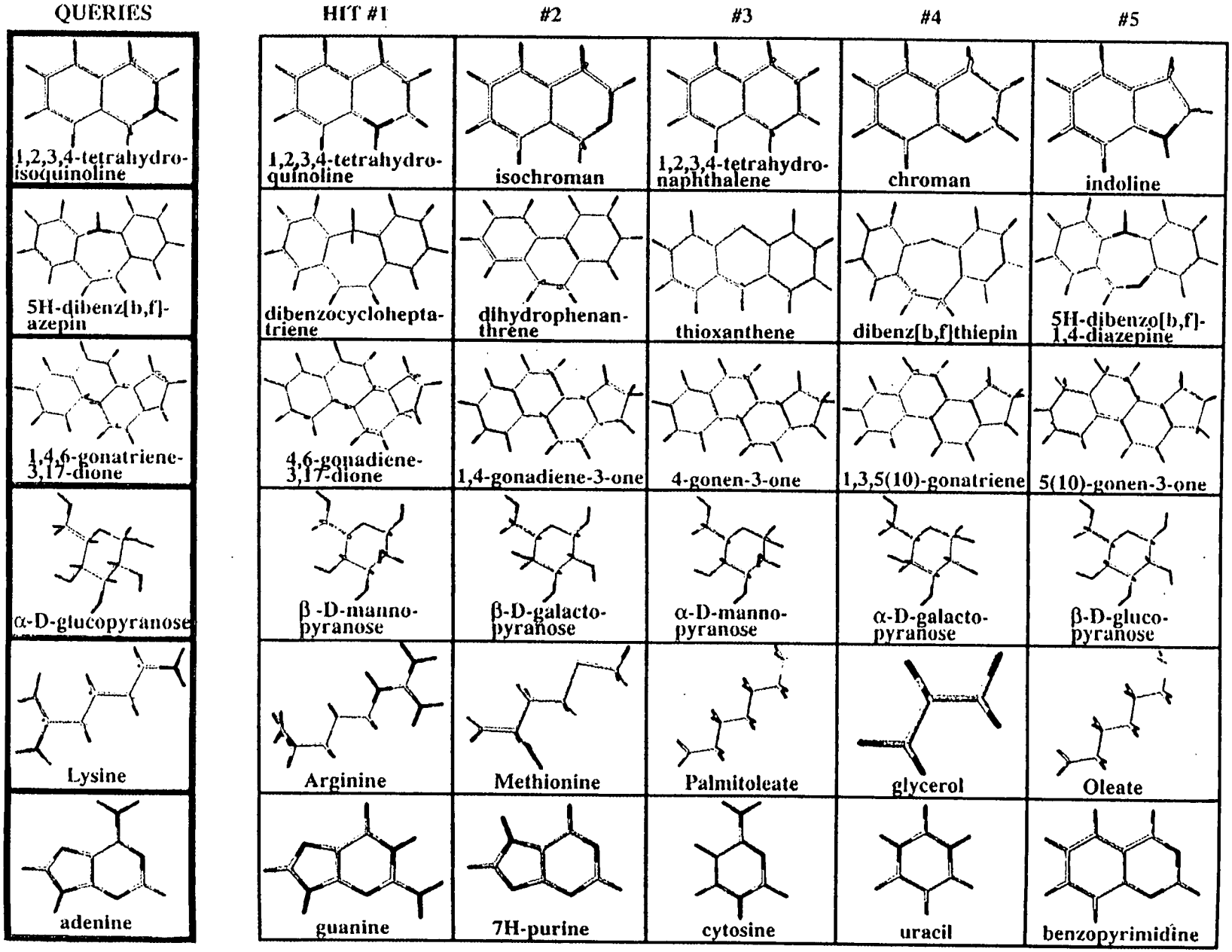
QUERY	Culling		No Culling	
	Hit	Score	Hit	Score
1,2,3,4-tetrahydroisoquinoline	1,2,3,4-tetrahydroquinoline	0.0370	1,2,3,4-tetrahydroquinoline	0.0173
	isochroman	0.0386	isochroman	0.0316
	1,2,3,4-tetrahydronaphthalene	0.0490	chroman	0.0399
	chroman	0.0574	1,2,3,4-tetrahydronaphthalene	0.0475
	indoline	0.0767	indan	0.0525
5H-dibenz[b,f]azepin	dibenzocycloheptatriene	0.0351	dibenzocycloheptatriene	0.0332
	dihydrophenanthrene	0.0482	dihydrophenanthrene	0.0384
	thioxanthene	0.0578	thioxanthene	0.0466
	dibenz[b,f]thiepin	0.0695	5H-dibenzo[b,f]-1,4diazepine	0.0487
	5H-dibenzo[b,f]-1,4-diazepine	0.0800	dibenz[b,f]thiepin	0.0578
1,4,6-gonatriene-3,17-dione	4,6-gonadiene-3,17-dione	0.0502	4,6-gonadiene-3,17-dione	0.0400
	1,4-gonadien-3-one	0.0743	1,4-gonadien-3-one	0.0660
	4-gonen-3-one	0.0984	4-gonen-3-one	0.0838
	1,3,5(10)-gonatriene	0.0986	1,3,5(10)-gonatriene	0.0862
	5(10)-gonen-3-one	0.1004	5(10)-gonen-3-one	0.0984
α-D-glucopyranose	β -D-mannopyranose	0.0417	α-D-mannopyranose	0.0376
	β-D-galactopyranose	0.0420	β -D-mannopyranose	0.0379
	α-D-mannopyranose	0.0559	β-D-galactopyranose	0.0391
	α-D-galactopyranose	0.0744	α-D-galactopyranose	0.0560
	β-D-glucopyranose	0.0748	β-D-glucopyranose	0.0766
Lysine	Arginine	0.0862	Methionine	0.0527
	Methionine	0.1024	Arginine	0.0821
	Palmitolenate(C16)	0.1163	Laurate(C12)	0.0959
	glycerol(-H)	0.1179	Palmitoleate(C16)	0.1004
	Oleate(C18)	0.1202	Myristate(C14)	0.1006
adenine	guanine	0.0626	guanine	0.0388
	7H-purine	0.0712	7H-purine	0.0701
	cytosine	0.0840	benzimidazole	0.0743
	uracil	0.0854	1H-indazole	0.0747
	benzopyrimidine	0.0860	benzoxazole	0.0775

FIG. 14A

Computer Aided Ligand-Based and Receptor-Based Drug Design Utilizing Molecular Shape
Inventor(s): Zauhar
Serial No. (if known): 10/635,280
Docket No. 30/1183US
Sheet 22 of 29

FIG. 14B

Results for Six Query Compounds, 1-D Shape Signature Self-Comparison of Tripos Fragment Database using L_1 Metric



Results for Six Query Compounds, 2D-MEP Shape Signature Self-Comparison of Tripos Fragment Database using L_1 Metric

QUERY	Culling		No Culling	
	Hit	Score	Hit	Score
1,2,3,4-tetrahydroisoquinoline	1,2,3,4-tetrahydroquinoline	0.0847	1,2,3,4-tetrahydroquinoline	0.0762
	1,2,3,4-tetrahydronaphthalene	0.1496	1,2,3,4-tetrahydronaphthalene	0.1307
	indoline	0.1732	indoline	0.1320
	acenaphthene	0.1908	indan	0.1554
	indan	0.2161	acenaphthene	0.1804
5H-dibenz[b,f]azepin	dibenzocycloheptatriene	0.1116	dibenzocycloheptatriene	0.1031
	acridan	0.2089	acridan	0.1538
	5H-dibenzo[b,f]-1,4-diazepine	0.2109	5H-dibenzo[b,f]-1,4-diazepine	0.1672
	1,2,3,4-tetrahydroisoquinoline	0.2268	phenanthridine	0.1762
	1,2,3,4-tetrahydroquinoline	0.2292	dihydrophenanthrene	0.1802
1,4,6-gonatriene-3,17-dione	4,6-gonadiene-3,17-dione	0.0888	4,6-gonadiene-3,17-dione	0.0852
	5a-gonane-3,17-dione	0.1383	5a-gonane-3,17-dione	0.1383
	1,4-gonadien-3-one	0.2028	1,4-gonadien-3-one	0.2097
	5a-gonan-3-one	0.2031	4-gonen-3-one	0.2122
	5a-gonan-17-one	0.2211	5a-gonan-3-one	0.2221
2-deoxy-β-D-ribofuranose	β-D-ribofuranose	0.2292	β-D-glucopyranose	0.2223
	β-D-glucopyranose	0.2368	α-D-fructofuranose	0.2317
	α-D-fructofuranose	0.2480	α-D-mannopyranose	0.2437
	α-D-galactopyranose	0.2616	β-D-ribofuranose	0.2445
	α-D-mannopyranose	0.2696	α-D-glucopyranose	0.2575
Lysine	Arginine	0.6615	Arginine	0.6617
	ethanolamine	0.7882	ethanolamine	0.7621
	choline	1.2682	choline	1.2442
	D-Threose	1.5332	D-Threose	1.4601
	D-Xylose	1.5667	D-Xylose	1.4912
adenine	pteridine	0.4025	benzothiazole	0.3493
	benzothiazole	0.4321	pteridine	0.3816
	guanine	0.4394	thiazole	0.3981
	7H-purine	0.4427	7H-purine	0.4254
	indene	0.4614	guanine	0.4265

FIG. 15

REPLACEMENT SHEET

Results for Six Query Compounds, 1D Shape Signature Comparison of Tripos Fragment Database against the NCI Database using L_1 and R_1 Metrics

QUERY	L_1 Metric		R_1 Metric	
	Hit	Score	Hit	Score
1,2,3,4-tetrahydroisoquinoline	91-21-4	0.0291	91-21-4	0.1153
	10500-57-9	0.0336	10500-57-9	0.1409
	529-35-1	0.0348	578-54-1	0.1428
	578-54-1	0.0380	493-05-0	0.1534
	24206-39-1	0.0397	529-35-1	0.1743
5H-dibenz[b,f]azepin	833-48-7	0.0324	833-48-7	0.1404
	1211-06-9	0.0360	1211-06-9	0.1673
	10354-00-4	0.0415	10354-00-4	0.1789
	82-53-1	0.0441	42263-75-2	0.2142
	6279-16-9	0.0488	51087-02-6	0.2300
1,4,6-gonatriene-3,17-dione	24640-00-4	0.0450	6126-58-5	0.2289
	10448-96-1	0.0556	24640-00-4	0.2561
	438-67-5	0.0570	6968-06-5	0.2672
	5976-74-9	0.0576	20919-82-8	0.2908
	6126-58-5	0.0584	3601-97-6	0.2963
α-D-glucopyranose	488-66-4	0.0546	74561-03-8	0.2223
	23559-36-6	0.0548	488-66-4	0.2548
	74561-03-8	0.0553	488-64-2	0.2548
	16505-91-2	0.0607	6623-68-3	0.2548
	39392-65-9	0.0655	2037-48-1	0.2549
Lysine	5329-79-3	0.0478	37149-01-2	0.1874
	110-97-4	0.0486	6963-39-9	0.1882
	5343-35-1	0.0552	110-97-4	0.2107
	37149-01-2	0.0555	6281-43-2	0.2201
	7356-00-5	0.0563	104-50-7	0.2224
adenine	10325-61-8	0.0271	10325-61-8	0.0944
	54346-27-9	0.0304	54346-27-9	0.0988
	73-24-5	0.0310	5426-35-7	0.1178
	1123-54-2	0.0343	73-24-5	0.1178
	2227-98-7	0.0353	19165-47-0	0.1178

FIG. 16A

Computer Aided Ligand-Based and Receptor-Based Drug Design Utilizing Molecular Shape
Inventor(s): Zauhar
Serial No. (if known): 10/635,280
Docket No. 30/7183US
Sheet 25 of 29

FIG. 16B

Results for Six Query Compounds, 1-D Shape Signature Comparison of Tripos Fragment Database vs. NCI

QUERIES	HIT #1	#2	#3	#4	#5
1,2,3,4-tetrahydro-isoquinoline	91-21-4	10500-57-9	529-35-1	578-54-1	24206-39-1
5H-dibenz[b,f]-azepin	833-48-7	1211-06-9	10354-00-4	82-53-1	6279-16-9
1,4,6-gonatriene-3,17-dione	24640-00-4	10448-96-1	438-67-5	5976-74-9	6126-58-5
α-D-glucopyranose	488-66-4	23559-36-6	74561-03-8	16505-91-2	39382-65-9
Lysine	5329-79-3	110-97-4	5343-35-1	37149-01-2	7356-00-5
adenine	10325-61-8	54346-27-9	73-24-5	1123-54-2	2227-98-7

. Results for Six Query Compounds, 2D-MEP Shape Signature Comparison of Tripos Fragment Database against the NCI Database using L_1 and R_1 Metrics

QUERY	L_1 Metric		R_1 Metric	
	Hit	Score	Hit	Score
1,2,3,4-tetrahydroisoquinoline	91-21-4	0.0701	91-21-4	0.5232
	635-46-1	0.0816	635-46-1	0.6553
	1484-19-1	0.0940	1484-19-1	0.6977
	1780-19-4	0.0983	5344-99-0	0.7295
	5344-99-0	0.1011	1780-19-4	0.8070
5H-dibenz[b,f]azepin	30646-39-0	0.0947	30646-39-0	0.8078
	16886-10-5	0.1079	3377-71-7	0.9075
	32446-13-2	0.1089	16886-10-5	0.9104
	3377-71-7	0.1126	32446-13-2	0.9166
	833-48-7	0.1167	833-48-7	0.9411
1,4,6-gonatriene-3,17-dione	56763-86-1	0.1524	20056-05-7	1.3418
	734-32-7	0.1645	56763-86-1	1.3451
	93998-31-3	0.1682	74924-17-7	1.4169
	20056-05-7	0.1693	734-32-7	1.4949
	74924-17-7	0.1702	71837-43-9	1.5131
α-D-glucopyranose	52019-14-4	0.1815	52019-14-4	1.4065
	49871-87-6	0.1833	58691-27-3	1.4270
	58691-27-3	0.1912	49871-87-6	1.4514
	7404-25-3	0.2015	2280-44-6	1.5418
	14215-77-1	0.2018	14215-77-1	1.5520
Lysine	42021-74-9	0.5473	85385-47-3	4.1381
	58048-33-2	0.5549	58048-33-2	4.2359
	58048-35-4	0.5684	42021-74-9	4.2441
	37082-52-3	0.5719	78582-26-0	4.3301
	78582-26-0	0.5721	62194-88-1	4.3458
adenine	73-24-5	0.0683	73-24-5	0.5048
	28128-33-8	0.1537	28128-33-8	1.0824
	7390-62-7	0.1581	7390-62-7	1.2106
	2846-89-1	0.1744	2846-89-1	1.2491
	3647-48-1	0.1820	1904-98-9	1.2947

FIG. 17A

REPLACEMENT SHEET

Results for Three Query Compounds, 2D-MEP Shape Signature, Tripos Fragment Database vs. NCI

QUERIES	HIT #1	#2	#3	#4	#5
1,2,3,4-tetrahydro-isoquinoline	91-21-4	635-46-1	1484-19-1	1780-19-4	5344-99-0
5H-dibenz[b,f]-azepin	39646-39-0	16886-10-5	32446-13-2	3377-71-7	833-48-7
adenine	73-24-5	28128-33-8	7390-62-7	2846-89-1	3647-48-1

FIG. 17B

REPLACEMENT SHEET

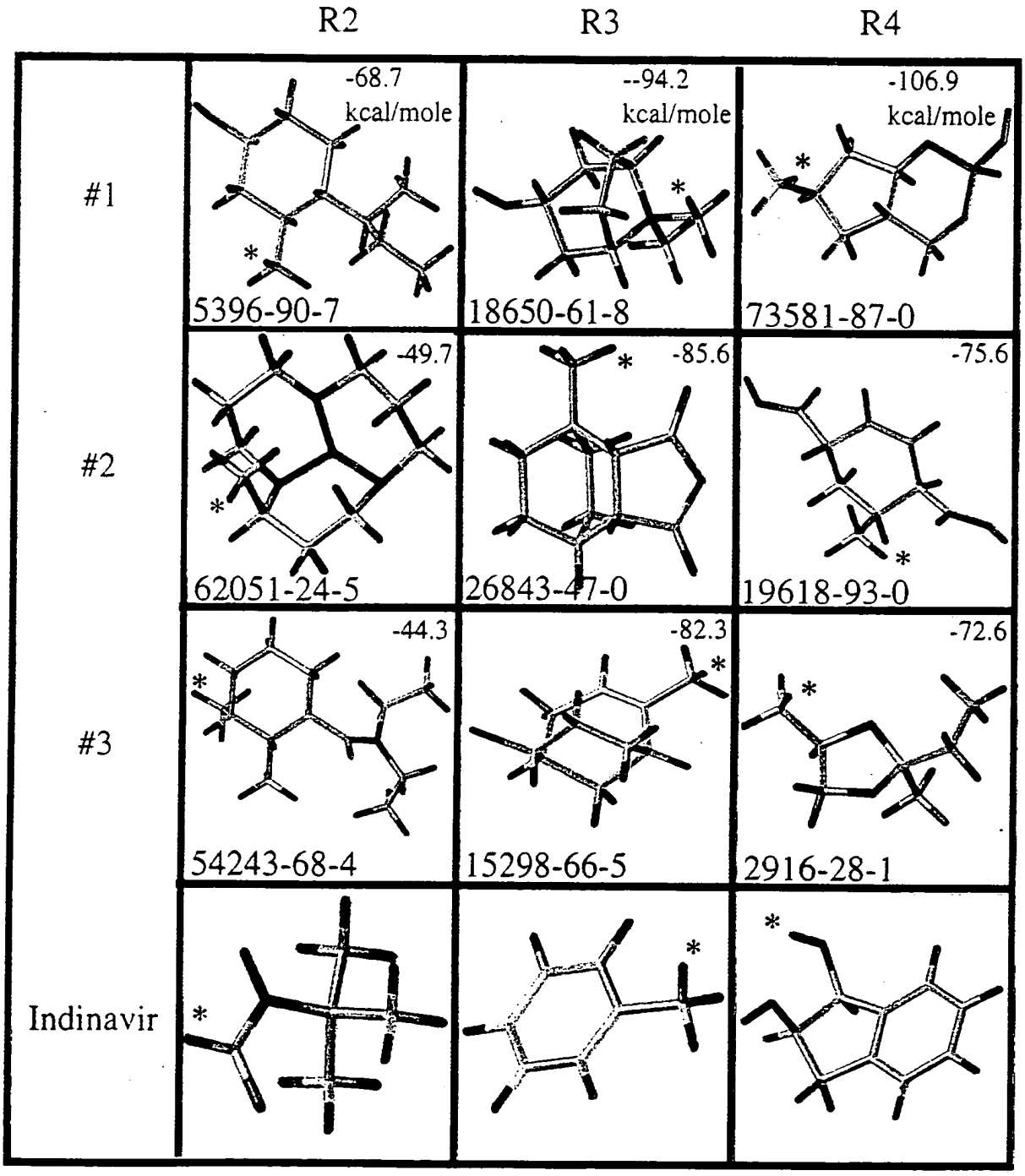


FIG. 18

REPLACEMENT SHEET

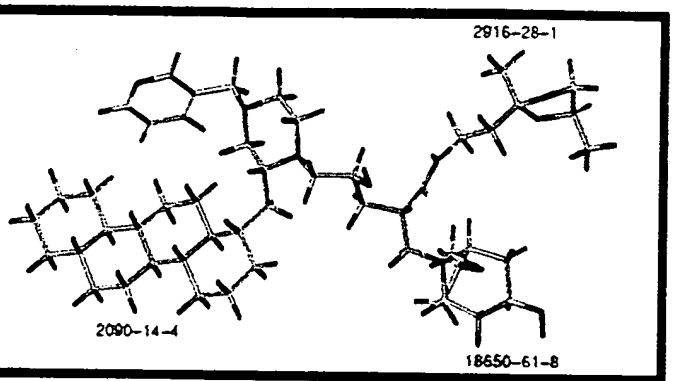
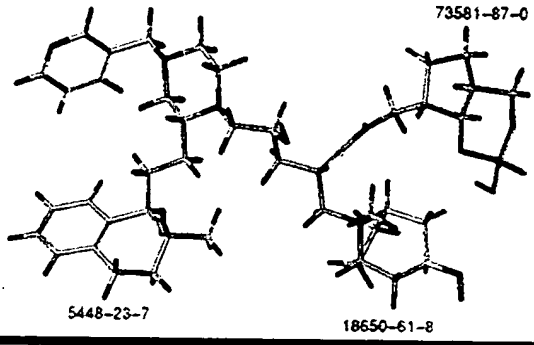
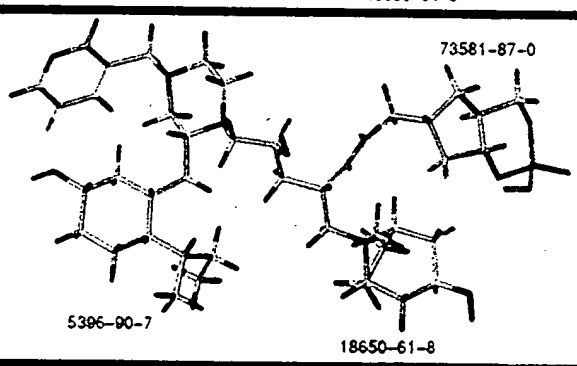
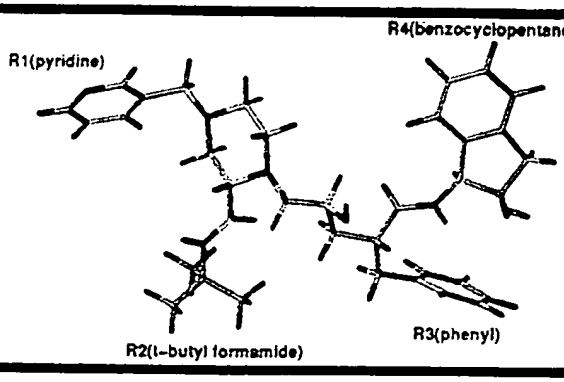
Rank	Energy(kcal/mol)	Structure
#1	-117.3	
#2	-117.0	
#4	-115.2	
Indinavir	-97.2	

FIG. 19